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PRELIMINARY AMENDMENT
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3. (Amended) A compound according to [Claim 1 or 2] <u>claim 1</u> wherein the target cell-specific portion is tumour cell-specific.

4. (Amended) A compound according to [any one of Claims 1 to 3] <u>claim 1</u> wherein the target cell-specific portion comprises an antibody or fragment or derivative.

5. (Amended) A compound according to [any one of Claims 1 to 3] <u>claim 1</u> wherein the target cell-specific portion comprises a macromolecule.

6. (Amended) A compound according to [any one of Claims 1 to 5] <u>claim 1</u> wherein the human NAD(P)H:quinone reductase 2 (NQO2) or a variant or fragment or fusion or derivative thereof is capable of being located substantially inside or following expression of the polynucleotide is located substantially inside the target cell.

7. (Amended) A compound according to [any one of Claims 1 to 6] <u>claim 1</u> comprising means for delivering said polynucleotide to said target cell.

8. A recombinant polynucleotide comprising a target cell-specific promoter operably linked to a polynucleotide encoding human NAD(P)(H):quinone reductase 2 (NQO2) or a variant or fragment or fusion or derivative thereof which has substantially the same activity as NQO2 towards a given prodrug.

9. (Amended) A recombinant polynucleotide according to [C]claim 8 wherein said promoter is tumour cell-specific.

10. (Amended) A recombinant polynucleotide according to [C]claim 8 [or 9] comprising a polynucleotide encoding NQO2.

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- 11. (Amended) A recombinant polynucleotide according to [any one of Claims 8 to 10] claim 8 which is capable, following expression in a target cell, of providing the NQO2 or a variant or fragment or fusion or derivative thereof located substantially inside the target cell.
- 12. (Amended) A compound according to [any one of Claims 1 to 7] <u>claim 1</u> wherein said polynucleotide is the recombinant polynucleotide of [any one of Claims 8 to 11] <u>claim 8</u>.
- one of Claims 1 to 7 or 12] <u>claim 1</u>, or a polynucleotide according to [any one of Claims 8 to 11] <u>claim 8</u> and a prodrug which is converted to a substantially cytotoxic drug by the action of NQO2.
- 14. (Amended) A system according to [C]claim 13 wherein the prodrug is CB 1954 or an analogue thereof.
- 15. (Amended) A system according to [C]claim 14 wherein the prodrug is CB 1954.
- 16. (Amended) A system according to [any one of Claims 13 to 15] <u>claim 13</u> further comprising a cosubstrate for NQO2.
- 17. (Amended) A system according to [C]claim 16 wherein the cosubstrate is nicotinamide riboside (reduced) (NRH) or an analogue thereof which can pass reducing equivalents to NQO2.





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- 18. (Amended) A method of treating a patient with a target cell to be destroyed the method comprising (a) administering to the patient a compound according to [any one of Claims 1 to 7 or 12] claim 1, or a recombinant polynucleotide according to [any one of Claims 8 to 11] claim 8; (b) allowing the NQO2 or a variant or fragment or fusion or derivative thereof to localize at, or be expressed in, the target cell; and (c) administering a prodrug which is converted to a substantially cytotoxic drug by the action of NQO2.
- 19. (Amended) A method according to [C]claim 18 wherein the patient has a tumour to be treated.
- 20. (Amended) A method according to [C]claim 18 [or 19] wherein the prodrug is CB 1954 or an analogue thereof.
- 21. (Amended) A method according to [C]claim 20 wherein the prodrug is CB 1954.
- 22. (Amended) A method according to [any one of Claims 18 to 21] claim 18 the method further comprising administering to the patient a cosubstrate for NQO2.
- 23. (Amended) A method according to [C]claim 22 wherein the cosubstrate is nicotinamide riboside (reduced) (NRH) or an analogue thereof which can pass reducing equivalents to NQO2.
- 24. (Amended) A compound according to [any one of Claims 1 to 7 or 12] claim 1, or a recombinant polynucleotide according to [any one of Claims 8 to 10] claim 8, for use in medicine.





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25. (Amended) Use of a compound according to [any one of Claims 1 to 7 or 12] claim 1, or a recombinant polynucleotide according to [any one of Claims 8 to 11] claim 8, in the manufacture of a medicament for treating a patient with a target cell to be destroyed.

26. (Amended) Use as defined in [C]claim 25 wherein the patient has been, is being or will be administered a prodrug which is converted to a substantially cytotoxic drug by the action of NQO2.

27. (Amended) Use of a prodrug which is converted to a substantially cytotoxic drug by the action of NQO2 in the manufacture of a medicament for treating a patient with a target cell to be destroyed wherein the patient has been, is being or will be administered a compound according to [any one of Claims 1 to 7 or 12] claim 1, or a recombinant polynucleotide according to [any one of Claims 8 to 11] claim 8.

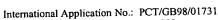
28. (Amended) Use as defined in [C]claim 27 wherein the patient has a tumour to be treated.

29. A method of treating a human patient with a target cell to be destroyed wherein the target cell expresses NQO2 the method comprising administering to the patient a prodrug which is converted to a substantially cytotoxic drug by the action of NQO2 and nicotinamide roboside (reduced) (NRH) or an analogue thereof which can pass reducing equivalents to NQO2.

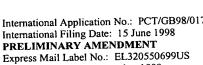
30. (Amended) A method according to [C]claim 29 wherein the cytotoxic drug is CB 1954 or an analogue thereof.

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- (Amended) A method according to [C]claim 29 [or 30] wherein the analogue 31. of NRH is able to permeate the target cellmembrane.
- (Amended) A method according to [any one of Claims 29 to 31] claim 29 32. wherein the target cell is a tumour.
- (Amended) A method according to [any one of Claims 29 to 32] claim 29 the 33. method further comprising determining, before administering the prodrug or NRH or an analogue thereof, whether the target cell to be treated expresses NQO2.
- A therapeutic system comprising a prodrug which is converted to a 34. substantially cytotoxic drug by the action of NQO2 and nicotinamide riboside (reduced) (NRH) or an analogue thereof which can pass reducing equivalents to NQO2.
- Nicotinamide riboside (reduced) (NRH) or an analogue thereof which can pass 35. reducing equivalents to NQO2 for use in medicine.
- Use of nicotinamide riboside (reduced) (NRH) or an analogue thereof which 36. can pass reducing equivalents to NQO2 in the manufacture of a medicament for treating a human patient with a target cell to be destroyed.
- (Amended) Use as defined in [C]claim 36 wherein the patient has been, is being or will be administered a prodrug which is converted to a substantially cytotoxic drug by the action of NQO2.
- Use of a prodrug which is converted to a substantially cytotoxic drug by the 38. action of NQO2 in the manufacture of a medicament for treating a human patient with a target cell to be destroyed wherein the patient has been, is being or will be administered NRH or an analogue thereof which can pass reducing equivalents to NQO2.